REMARKS

Claims 1-127 are pending in the current application. Claim 95 has been amended to be dependent from Claim 1 to correct an error of multiple dependency. Claims 100 and 112 have been cancelled as unacceptable multiple dependent claims. Claims 102 and 114 have been cancelled since they were dependent from cancelled claims 100 and 112, respectively.

The subject matter of Claims 104 and 116 have been incorporated into Claims 99 and 111, respectively.

Objections to the Specification

I. The title was objected to as being non-descriptive.

Applicants respectfully submit that the replacement of the current tile with the new title renders the rejection moot.

35 USC §112 Rejections

I. Claims 99-103, 106-109, 111-115 and 118-122 were rejected under 35 USC §112, 2nd paragraph, as being indefinite.

Applicant respectfully submits that the incorporation of the subject matter from Claims 104 and 116 into Claims 99, 106, 111 and 118, renders the rejection moot.

II. Claims 1-127 were rejected under 35 USC §112, 1st paragraph, as being non-enabling for solvates and prodrugs.

Examiner acknowledges that the specification is enabling for pharmaceutically acceptable salts but asserts that hydrates, solvates and prodrugs are not sufficiently enabled. Applicant respectfully disagrees.

Examiner asserts that no specific solvates are mentioned. This is not true. Hydrates are a subclass of solvates where the solvent is water. In the definition section, the following definition is provided.

> "The term "solvate" refers to a molecular complex of a compound represented by Formula (I) or (II) (including prodrugs and pharmaceutically acceptable salts thereof) with one or more solvent molecules. *Such solvent molecules are those commonly used in the pharmaceutical art, which are known to be innocuous to the recipient, e.g.,* ***water, ethanol***, and the like." (emphasis added) Page 35, lines 25-29

The term "solvate" is discussed again on page 52, lines 4-7.

> "The compounds of the present invention may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as ***water, ethanol***, and the like, and it is intended that the invention embrace both solvated and unsolvated forms." (emphasis added)

Examiner goes on to assert that there is no working example of any prodrug, hydrate, or solvate formed and no direction for making any solvate is disclosed. It is well established that an inventor is not required to exemplify every species and/or embodiment of his/her invention. In fact, there is no requirement to provide any working examples. To satisfy the enablement requirement, one must provide sufficient information to enable one of ordinary skill in the art to practice the invention. To include every minute detail in the specification would be superfluous and make it difficult to identify the new or important aspects of the invention. More importantly, it is not necessary to describe procedures that are well-known in the art. The preparation of solvates of organic compounds is routine in the art as evidenced by Polymorphism in Pharmaceutical Solids, Ed. Harry G. Brittan, Vol 95, Marcel Dekker, Inc., New York, 1999 (referred to herein as "Brittan reference"). For example, Chapter 5 entitled "Generation of Polymorphs, Hydrates, Solvates and Amorphous Solids" on pages 202-208 of the Brittan reference (attached hereto) describes how solvates of both organic and inorganic compounds are routinely prepared. In addition, methods for the characterization of such forms are also discussed.

Examiner relies on a phrase taken from a "Solid State Chemistry" text. However, Examiner is assuming that all solvates are solids. They are not. Applicant defines solvates as "a molecular complex of a compound represented by Formula (I) or (II) (including prodrugs and pharmaceutically acceptable salts thereof) with one or more solvent molecules." Nothing in this definition requires the solvate to be a solid. Applicant would like to remind Examiner that a liquid solution is a solvated form of a compound. Even though it may be difficult to predict a specific stoichiometry formed by a solid solvate, Applicant is not claiming a specific stoichiometry. Therefore, it is unreasonable for Examiner to limit Applicant's claims simply because he has not identified all the specific forms of solvates/hydrates that inherently form.

Contrary to Examiner's statement that the breadth of solvents is overly broad, Applicant would like to remind Examiner that the specification defines the solvents as those that are *commonly used in the pharmaceutical art, which are known to be innocuous to the recipient.* Applicant respectfully submits that this is not overly broad since the regulatory agencies limit the solvents that are considered "innocuous" to the

recipient.

Since it is well established in the law that a specification is not required to include routine processes for enablement, Applicants respectfully submits that the disclosure is sufficiently enabling and the Examiner has provided no evidence to the contrary.

Examiner also stated that prodrugs would be acceptable if the definition in the specification was incorporated into the claim. Applicant has amended Claim 1 (the only instance of the use prodrug) to eliminate the term since prodrugs are already incompassed within the definitions of the various groups that would provide useful prodrugs.

III. Claims 1-8, 11-16, 20-24, 27-32, 36-40, 43-45, 48-82, 84-86, 88-93, 95-127 were rejected under 35 USC 35 §112, 1st paragraph for non-enablement of all compounds claimed.

Examiner asserts that the specification does not reasonably provide enablement for "using" the compounds of formula (I) with R^0 and R^1 = substituted aryl generally or heteroaryl. Applicant respectfully disagrees. Examiner appears to be confusing utility with enablement. Applicant provides more than sufficient information on how to make the compounds of Formula (I) as claimed. In addition, Applicant would also like to remind the Examiner that he can rely on the state of the art. At the time of filing the present application, evidence existed that the chloro-substituted phenyl rings could be substituted with other aryl or heteroaryl groups in compounds that act as CB-1 receptor antagonists. See, e.g., US Publication No. 2004/0092520 (Example 18) by the inventor. Therefore, it would have been reasonable for the inventor to believe that other substituted phenyl and heteroaryl groups would perform as claimed.

More importantly, Applicant would like to point out to the Examiner that controlling precedent requires that the US PTO accept the objective truth of Applicant's teachings of enablement unless there is a reason to doubt these teachings. Applicant respectfully submits that there is no reason to doubt the objective truth of the statements contained within the Specification upon which Applicant relies for enabling support.

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing the defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for

the enabling support. In Re Marzocchi, 439 F.2d 220,222 (CCPA 1971).

The burden is on the Examiner to come forward with *evidence* as to why assertions of utility should not be accepted. In the instant case, the Examiner has merely made conclusory statements without any specific evidence why Applicant's assertions should not be accepted as true. Without such supporting information, the rejection of the specification/claims under 35 USC §112, 1st paragraph for lack of enablement is contrary to well established law.

IV. Claims 99-122 were rejected under 35 USC§112, 1st paragraph for non-enablement for all claimed indications.

Examiner acknowledges that compounds that antagonize the CB-1 receptor have been shown to be useful for the treatment of obesity. Applicant respectfully submits that the other indications listed in the amended claims have also been shown to be treatable by compounds that act as CB-1 receptor antagonists (or inverse agonists). See, references listed in the table below.

Indication	**Reference**
Weight Loss, Obesity, Bulimia	Brodie, B.B., "Rimonabant: The first therapeutically relevant cannabinoid antagonist," Life Sciences, **77** 2339-2350 (2005). Chambers, A.P., et al., "Cannabinoid (CB1) receptor antagonist, AM251, causes a sustained reduction of daily food intake in the rat," Physiology & Behavior, **82**, 863-869 (2004). Smith, R.A., "Recent advances in the research and development of CB1 antagonists, IDrugs, **8**(1), 53-66 (2005). Van Gaal, L.F., et al., "Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients : 1-year experience from the RIO Europe study, " Lancet, **365**, 1389-1397 (2005).
Depression Atypical Depression	Witkin, J.M., "A therapeutic role for cannabinoid CB1 receptor antagonists in major depressive disorders," Trends in Pharmacological Sciences, **26**(12), 609-617 (2005). Griebel, G., et al., "Effects of the Cannabinoid CB1 Receptor Antagonist Rimonabant in Models of Emotional Reactivity in Rodents," Biol. Psychiatry, **57**(3) 261-167 (2005).

Bipolar Disorders Psychoses Schizophrenia	Poncelet, M., "Blockade of cannabinoid (CB1) receptors by SR141716 selectively antagonized drug-induced reinstatement of exploratory behaviour in gerbils," Psychopharmacology, **144**, 144-150 (1999). Fernandez, J.R., et al. « Rimonabant Sanofi-Synthelabo », 5(4), 430-435 (2004).
Behavioral Additions, Suppression of Reward-related Behaviors	DeVries, T.J., "Cannabinoid CB1 receptors control conditioned drug seeking," Trends in Pharmacological Sciences, **26**(8), 420-406 (2005). Brodie, B.B., "Rimonabant: The first therapeutically relevant cannabinoid antagonist," Life Sciences, **77** 2339-2350 (2005). Mas-Nieto, M., et al., "Reduction of opioid dependence by the CB1 antagonist SR141716A in mice: evaluation of the interest in pharmacotherapy of opioid addiction," British Journal of Pharmacology, **132**, 1809-1816 (2001). Chaperon, F., "Involvement of central cannabinoid (CB1) receptors in the establishment of place conditioning in rats," Psychopharmacology, **135**, 324-332 (1998). Sanudo-Pena, M.C., et al., "Endogenous cannabinoids as an aversive or counter-rewarding system in the rat," Neuroscience Letters, **223**, 125-128 (1997). Mansbach, R.S., "Effects on the cannabinoid CB1 receptor antagonist SR171716 on the behavior of pigeons and rats," Psychopharmacology, **124**, 315-322 (1996).
Alcoholism	Mechoulam, R., et al., "Cannabis and alcohol – a close friendship," TRENDS in Pharmacological Sciences, **24**(6), 266-268 (2003).
Tobacco Abuse	Cohen, C., et al., "SR141716, a central cannabinoid (CB1) receptor antagonist, blocks the motivational and dopamine-releasing effects of nicotine in rats," Behavioural Pharmacology, **13**, 451-463 (2002). Le Foll, B., et al., "Rimonabant, a CB1 antagonist, blocks nicotin-conditioned place preferences," NeuroReport, **15**(13), 2139-2143 (2004).
Dementia	Wolff, M.C., et al., "SR141716A, a cannabinoid CB1 receptor antagonist, improves memory in a delayed radial maze task," European Journal of Pharmacology, **477**, 213-217 (2003).
Attention Deficit Disorder	Louis, C., et al., "Surinabant, a New CB1 Receptor Antagonist, Displays Efficacy in Animal Models of Attention Deficit/Hyperactivity Disorder" Psychopharmacology, **30**(Supple.1), S173, Abstract 77, (2005).
Parkinson's Disease	Di Marzo, V., et al., "Enhanced levels of endogenous cannabinoids in the globus pallidus are associated with a

	reduction in movement in an animal model of Parkinson's disease," FASEB Journal, **14**, 1432-1438 (2000). Ferrer, B., et al., "Effects of levodopa on endocannabinoid levels in rat basal ganglia: implications for the treatment of levodopa-induced dyskinesias," European Journal of Neuroscience, **18**, 1607-1614 (2003). Van der Stelt, M., et al., "A role for endocannabinoids in the generation of parkinsonism and levodopa-induced dyskinesia in MPTP-lesioned non-human primate models of Parkinson's disease," FASEB Journal, **19**(9), 1140-1142 (2005).
Inflammation	US Provisional Patent Application No. 60/723493 filed on October 3, 2005.
Gastrointestinal Disorders	Croci, T., et al., "Role of cannabinoid CB1 receptors and tumor necrosis factor-α in the gut and systemic anti-inflammatory activity of SR141716 (Rimonabant) in rodents," British Journal of Pharmacology, **140**, 115-122 (2003).
Type II Diabetes	Bermudez-Siva, F.J., et al., "Activation of cannabinoid CB1 receptors induces glucose intolerance in rats, " European Journal of Pharmacology, **531**, 282-284 (2006). Pagotto, U., et al., "The role of the endocannabinoid pathway in metabolism and diabetes," Current Opinion in Endocrinology & Diabetes, **13**, 171-178 (2006).

It would be reasonable for one to believe if a particular CB-1 antagonist can be used to treat a particular disease, condition or disorder, then other CB-1 antagonists should behave similarly. Applicant respectfully submits that the references listed above provide more than ample evidence that a CB-1 antagonist would be useful for the claimed indications.

35 USC §102 Rejections

I. Claims 1, 2, 95 and 96 were rejected under 35 USC §102(e) as being anticipated by Gudmundsson (US Publication No. 2005/0203106).

Applicant respectfully submits that the amendment of Claim 1 to limit the definition of R^1 to an optionally substituted aryl renders the rejection moot.

II. Claim 123 was rejected under 35 USC §102(b) as being anticipated by Taujitani (US Patent No. 4,992,442).

Applicant respectfully submits that the amendment of Claim 123 to limit the definition of R^0 to substituted aryl groups renders the rejection moot.

III. Claim 123 was rejected under 35 USC §102(e) as being anticipated by Gudmundsson (US Publication No. 2005/0203106).

Applicant respectfully submits that the amendment of Claim 123 to limit the definition of R^0 to the preferred substituted aryl groups (2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl) renders the rejection moot.

IV. Claim 124 was rejected under 35 USC §102(e) as being anticipated by Gudmundsson (US Publication No. 2005/0203106).

Applicant respectfully submits that the amendment of Claim 124 to limit the definition of R^0 to the preferred substituted aryl groups (2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl) renders the rejection moot.

V. Claim 126 was rejected under 35 USC §102(b) as being anticipated by Inoue (JP 05/125079).

Applicant respectfully submits that the amendment of Claim 126 to limit the definition of R^0 to an optionally substituted aryl renders the rejection moot.

VI. Claim 126 was rejected under 35 USC §102(b) as being anticipated by Inoue (US Patent No. 5,843,951).

Applicant respectfully submits that the amendment of Claim 126 to limit the definition of R^0 to the preferred substituted aryl groups (2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl) renders the rejection moot.

35 USC §103 Rejections

I. Claim 125 was rejected under 35 USC §103(a) as being unpatentable over Gudmundsson (US Publication No. 2005/0203106).

Examiner asserts that Gudmundsson teaches a compound with bromine in position 3 of the pyrazolo[1,5-1-pyrimidine ring and it would be obvious to substitute the bromo group with an iodo group. It is important to note that the compounds taught by Gudmundsson are for the treatment of herpes viral infections which is totally unrelated to

the present invention. In addition, Gudmundsson provides no teachings or suggestions that an intermediate where R^0 is 2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl would have any benefit. Consequently, Applicant respectfully submits that the amendment of Claim 125 to those compounds where R^0 is 2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl renders the rejection moot.

Respectfully Submitted:

Date: July 7, 2006

Arlene K. Musser
Attorney for Applicants
Registration No. 37,895

Pfizer Inc.
Patent Department, MS: 8260-1611
Eastern Point Road
Groton, Connecticut 06340
(860) 715-0871